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Cardiovascular Disease

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Disorders of the circulatory system cover a broad range. We focus in this chapter on four chronic vascular diseases for which atherosclerosis and/or hypertension are the defining characteristics. These are coronary heart disease (CHD), stroke, peripheral vascular disease, and hypertensive heart disease. The reasons for this are several. First, these conditions are the most important cardiovascular diseases (CVDs) in industrial countries, accounting for half of mortality in North America and Europe. Second, they are already quite prevalent in developing countries, contributing approximately 16 percent of deaths (WHO MONICA Project 1989). Indeed, it has been observed that the majority of the world's cases of cardiovascular disease no longer occur in industrial nations but, rather, in developing countries (figure 23-1); demographic analyses, summarized in this chapter (table 23-3), confirm this view. Third, they have some risk factors in common and, thus, share preventive strategies. Indeed, in those industrial countries experiencing declining cardiovascular mortality rates, most of the declines in total mortality could be attributed to declines in CVD. Fourth, a great deal is known about the pathogenesis, risk factors, prevention, and treatment of these conditions, allowing priorities to be set regarding preventive and therapeutic interventions.

Several important cardiovascular diseases have not been included in this chapter. These include rheumatic heart disease, cor pulmonale, congenital heart diseases, and cardiomyopathies. Rheumatic heart disease remains a worldwide problem, especially in developing nations; Chapter 10 of this collection (Rheumatic Heart Disease) provides a review of the main issues concerning this condition. Cor pulmonale results principally from chronic obstructive pulmonary disease and is, therefore, discussed in the chapter on that subject by Bumgarner and Speizer (chapter 24, this collection). Little is known about the causes and preventability of congenital heart disease, with the exception of rubella-related disease, and, therefore, these conditions are not dealt with in this collection. Finally, cardiomyopathies are regionally, rather than globally, important (for example, Keshan disease in China, Chagas' disease in South America, West African cardiomyopathy). These conditions are beyond the scope of the chapters in this collection. Hutt (1991) provides an overview, with extensive references, of these more traditional patterns of cardiovascular diseases in Africa.

Atherosclerosis and Hypertension

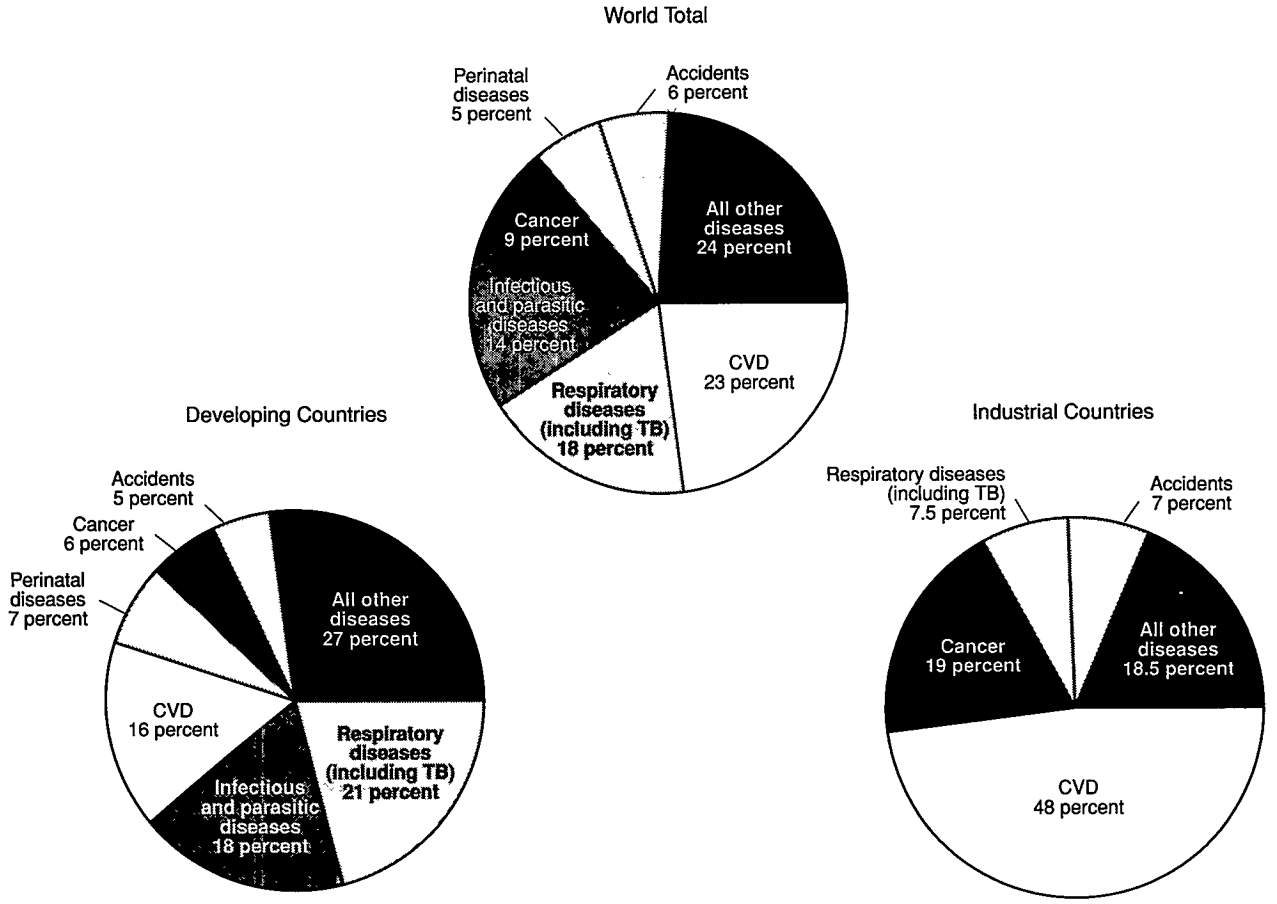
We begin this chapter with a brief discussion of the etiology and pathogenesis of atherosclerotic and hypertensive cardiovascular disease, emphasizing the role of modifiable risk factors as targets for preventive strategies. We then review trends in these diseases, making projections into the twenty-first century. Finally, we discuss preventive and case management strategies as appropriate to countries with limited health care resources.

Etiology and Pathogenesis of Atherosclerosis

Atherosclerosis is a chronic vascular condition characterized by focal accumulations of smooth muscle cells, collagen, and lipids in medium and large arteries. The condition may begin as early as childhood, initiated by injury to the endothelial lining of these major arteries, exposing the subintimal smooth muscle cells and macrophages to serum lipoproteins, platelets, and other constituents (Ross 1986). These in turn stimulate the proliferation of the smooth muscle cells and the focal accumulation of lipids. Initially, small, flat fatty streaks are observed. Previous studies have noted rather high prevalence of these lesions in autopsy studies even in developing countries (McGill 1968). If cellular proliferation continues, there may be growth into the lumen of the artery, forming the lesion pathognomonic of atherosclerosis, the fibrous-capped plaque. Tracey and Toca (1975) found that, at least in the 1960s, these lesions were much less prevalent in developing than industrial countries. Evidence has long suggested that fatty streaks can undergo regression; some recent evidence has suggested that even fibrous-capped plaques can regress, though this point is controversial (Blankenhorn and others 1987).

CLINICAL SYNDROMES RELATED TO ATHEROSCLEROSIS. Angina pectoris, myocardial infarction, sudden death, transient ischemic attacks, atherothrombotic stroke, aortic aneurysm, and intermittent claudication are all related to atherosclerosis and

Figure 23-1. Estimated Distribution of Causes of Death, 1980



TB = Tuberculosis
Note: Of the total deaths, 78 percent are in developing countries.
Source: Authors' compilation; WHO MONICA Project, 1989.

its complications. When the atherosclerotic plaque occludes the lumen to the extent that blood flow is impaired, any increased demand for blood flow (such as that brought about by exertion) will lead to deficiency of oxygen and nutrients to the organ supplied. When the coronary arteries are narrowed, chest pain (angina pectoris) occurs; when the peripheral arteries are narrowed, intermittent claudication occurs. Plaques may undergo complication when the fibrous cap ulcerates, ruptures, or forms a clot. Subacutely, this can result in unstable angina in the coronary circulation or transient ischemic attacks in the cerebral circulation. Complete occlusion of the coronary artery with thrombosis then leads to myocardial infarction; occlusion or embolism in the cerebral circulation leads to atherothrombotic stroke. Myocardial oxygen deprivation from arterial stenosis or occlusion can also cause a variety of cardiac arrhythmias, including those causing cardiovascular collapse and sudden death. Myocardium damaged by infarction may be unable to maintain cardiac output, leading to congestive heart failure. Atherosclerotic involvement of the aorta can lead to a weakening of the arterial wall, resulting in aortic aneurysm and aortic dissection.

Hypertension-Related Diseases: Etiology and Pathogenesis

The end organs affected most by elevated blood pressure include the arteries, the heart, and the kidneys. Hypertension is a risk factor for atherosclerosis. Furthermore, hypertension is thought to play a significant role in weakening the arterial wall in the cerebral circulation, leading to cerebral hemorrhage. Though the sequence of events is controversial, cardiac hypertrophy is strongly associated with hypertension. Severe cardiac hypertrophy impairs the heart's ability to fill with blood, resulting in congestive heart failure. The increased myocardial mass interacts with atherosclerotic disease to predispose to infarction and arrhythmia. The arteries of the kidneys are susceptible to medial and intimal hypertrophy, known as nephrosclerosis, a common cause of chronic renal failure.

The Role of Risk Factors

The pathogenesis of vascular disease is summarized in figure 23-2. These so-called risk factors have been associated with the clinical cardiovascular syndromes, usually in epidemiologic

Figure 23-2. The Pathogenesis of Atherosclerotic Vascular Diseases

Source: Authors' compilation.

studies. The other point illustrated in figure 23-2 is that some risk factors act to cause atherosclerosis, whereas others act after the formation of the atherosclerotic plaques to cause the complications (thrombosis, hemorrhage, and so on) which present as clinical syndromes.

There are several practical implications of these roles for risk factors. First, risk factors causing the formation of atherosclerotic plaques would be logical targets for primary prevention efforts. Those risk factors acting after the formation of atherosclerosis should be modified in secondary prevention efforts. Second, it is conceivable that in certain populations which do not develop atherosclerotic plaques, certain risk factors may not be as important as in other atherosclerosis-prone groups.

As demonstrated in table 23-1, most of the important cardiovascular diseases share important risk factors. An example of this is the powerful effect of elevated blood pressure in increasing relative risk for both stroke and coronary heart disease, as is illustrated in figure 23-3. (Notice that risk for both conditions rises over the range of even "normal" values of diastolic blood pressure [DBP], suggesting, thereby, the limited usefulness of specific cutoff values to define "hypertension.") Thus, reduction in one or more risk factors may prevent several cardiovascular diseases. Several general comments are in order. First, the multifactorial nature of the etiology of cardiovascular disease makes complex the development and evaluation of preventive strategies; multifactorial interventions may be necessary to maximize the effect of preventive efforts. Second, the relative strength of association differs between diseases such that control of a risk factor may be more important for the control of one vascular disease than another. This may also be true for specific cardiovascular diseases within different racial and ethnic groups. For example, the relative risk of hypertension as in cases of stroke appeared higher in American blacks than American whites. Third, some of the risk factors are modifiable, whereas others are not. The physiological risk factors are only indirectly modifiable, through change in the behavioral ones; they thus serve principally as indicators to spur behavior change (or medical intervention) and as measures of progress. Fourth, in contrast to many other conditions, there appear to be no important environmental or infectious

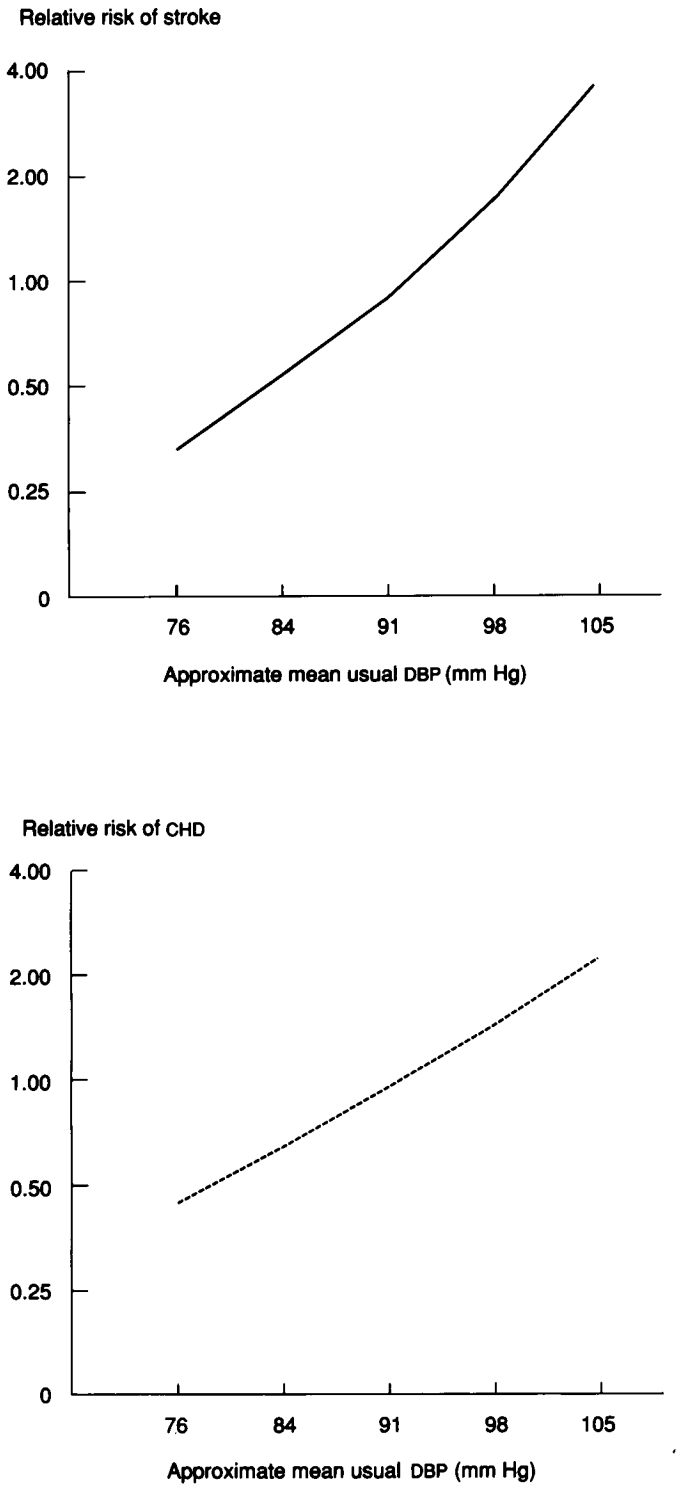
Table 23-1. Association between Risk Factors and Cardiovascular Diseases

	Degree of association				
Risk factor	*Coronary heart disease*	*Atherothrombotic stroke*	*Peripheral vascular disease*	*Hemorrhagic stroke*	*Hypertensive heart disease*
Nonmodifiable					
Age	++++	++++	++++	++++	++++
Male sex	++++	++++	++++	++++	+
Black race	+	+ +	?	+++	+++
Family history	++++	+ +	+ +	+ +	+ +
Modifiable physiological					
Elevated LDL(low-density lipoprotein)	++++	+ +	+++	–	0
Decreased HDL(high-density lipoprotein)	++++	+	+ +	0	0
Hypertension	+++	+ +	+ +	++++	++++
Diabetes	+++	+++	++++	0	0
Obesity	+ +	?	?	?	+
Behavioral					
Smoking	+++	+ +	++++	0	0
Dietary cholesterol and saturated fat	+ +	+	+ +	–	–
Salt consumption	0	+	0	+ +	+ +
Alcohol consumption	–	+	–	+	+
Sedentary lifestyle	+ +	?	?	0	+

Key: ++++ Strong association between disease and risk factor.
+++ Moderately strong association between disease and risk factor.
++ Moderate association between disease and risk factor.
+ Weak association between disease and risk factor.
0 No association between disease and risk factor.
+/– Association varies with the level of the risk factor.
? Unclear association between disease and risk factor.
– Inverse association between disease and risk factor.

Source: Authors.

Figure 23-3. Diastolic Blood Pressure and the Risk for Stroke and Coronary Heart Disease



Note: Stroke risk based on seven prospective observational studies with 843 events. CHD risk based on nine prospective observational studies with 4,856 events. The five baseline DBP categories are estimated from remeasurements in the Framingham study.
Source: MacMahon and others 1990.

risk factors, with the possible exceptions of water hardness (WHO 1982, p. 33) and cytomegalovirus infection (Melnick, Adam, and DeBakey, 1990). Fifth, males are at substantially higher risk than females, although to different extents for different diseases. In table 23A-1 we summarize MONICA (Monitoring Trends and Determinants in Cardiovascular Disease Project) mortality data that suggest a very strong effect for ischemic heart disease and a much weaker one for stroke; indeed, as a proportion of overall mortality, males appear less affected by stroke than females. Although race, sex, and age are obviously unmodifiable, their importance suggests the need for specific modeling of other risk factor effects for these characteristics.

THE ORIGIN OF RISK FACTORS. A useful concept is that of the "proximal" risk factor; that is, the factor which causes the development of the risk factors (table 23-2). Several points deserve emphasis. First, age is related to most risk factors. Second, several risk factors are transmitted genetically, rendering a subgroup of the population at high risk regardless of their lifestyles. Third, other risk factors may cause the development of certain risk factors (for example, smoking is related to low high-density lipoprotein [HDL] cholesterol), and some of the effect of one risk factor may be mediated through another risk factor. Fourth, as reflected in table 23-1, a number of the risk factors are physiologic, which, in turn, appear to be related to behavioral or lifestyle factors (for example, smoking and sedentary lifestyle are related to low HDL cholesterol). Thus, alteration of these behaviors may control the risk factor, even if it has never been clinically identified. Finally, risk factors tend to cluster within individuals as a result of behavioral or genetic mechanisms. Thus, the treatment of risk factors must often take these coexisting risk factors into account.

The multifactorial nature of etiology of cardiovascular disease and the interrelated nature of the most important risk factors makes for a rich and complex range of possibilities in the development of preventive strategies. In practical application, both the alteration of human behaviors leading to the risk factors (the population-based strategy) and the clinical treatment of those with high-risk factor levels (the high-risk strategy) may be more straightforward strategies to reduce cardiovascular risk. When the population-based strategy is implemented before risk factors become highly prevalent in a population, it is called primordial prevention (Dodu 1984, 1988).

The preceding discussion can, perhaps, best be summarized in a diagram (figure 23-4) that shows a (simplified) scheme of the relationships among groups of risk factors and end points. Policy instruments per se are not shown in the figure, but they divide naturally into those that operate through the behavioral risk factors (for example, antismoking campaigns and taxes on fatty meat products) and medical interventions that operate directly on physiological risk factors (such as medication that lowers cholesterol). Emphasis on one policy or the other may differ between population subgroups, depending on the prevalence and relative risk of the risk factors.

Table 23-2. Association between Nonmodifiable and Behavioral Risk Factors and Development of Physiological Risk Factors

	Degree of association				
Nonmodifiable and behavioral risk factors	*Elevated LDL*	*Decreased HDL*	*Hypertension*	*Diabetes*	*Obesity*
Nonmodifiable					
Age	+ +	–	+	+	+
Male sex	–	+ +	–	–	–
Black race	–	P	++++	++[a]	+ +[a]
Family history	++++	+ +	+++	+	+ +
Behavioral					
Smoking	–	+ +	–	–	–
Dietary saturated fat	+++	–	+	–	+
Dietary calories	+	+ +	+ +	+ +	++++
Salt consumption	–	–	+++	–	–
Alcohol consumption	–	P	+ +	–	+
Sedentary lifestyle	–	+ +	+ +	+ +	+++

a. Women only.
Key: +++ Strong association.
+++ Moderately strong association.
++ Moderate association.
+ Weak association.
– No association.
P Protective association.
Source: Authors' compilation.

The breadth and sophistication of current epidemiologic knowledge of the etiology of cardiovascular disease is a scientific triumph of the past two decades. This knowledge provides the tools for prevention that have been applied, with remarkable success, in several high-income countries. Applying this knowledge in a developing country remains a central challenge.

Clinical Presentation and Mortality Rates

This section reviews the available data for the specific diseases.

CORONARY HEART DISEASE. As mentioned previously, coronary heart disease can present as angina pectoris, myocardial infarction, or sudden cardiac death. If worldwide proportions are similar to those in the United States, approximately 40 percent of coronary disease presents as angina pectoris, 40 percent as myocardial infarction, and 20 percent results in sudden cardiac death (death within one hour of onset of symptoms [Kannel and Feinleib 1972]). Because as many as 20 percent of the myocardial infarction victims will die in the hospital (in addition to the victims of sudden death) and a significant portion will remain disabled after infarction, primary prevention is an obviously important objective. The reduction in case-fatality rates following infarction and the prevention of infarction or sudden death in angina patients would be important goals in secondary prevention. It should be pointed out that any reduction in case-fatality rates for myocardial infarction would yield prevalent cases of coronary disease, requiring great expenditure of health resources. This again emphasizes the need for primary prevention strategies.

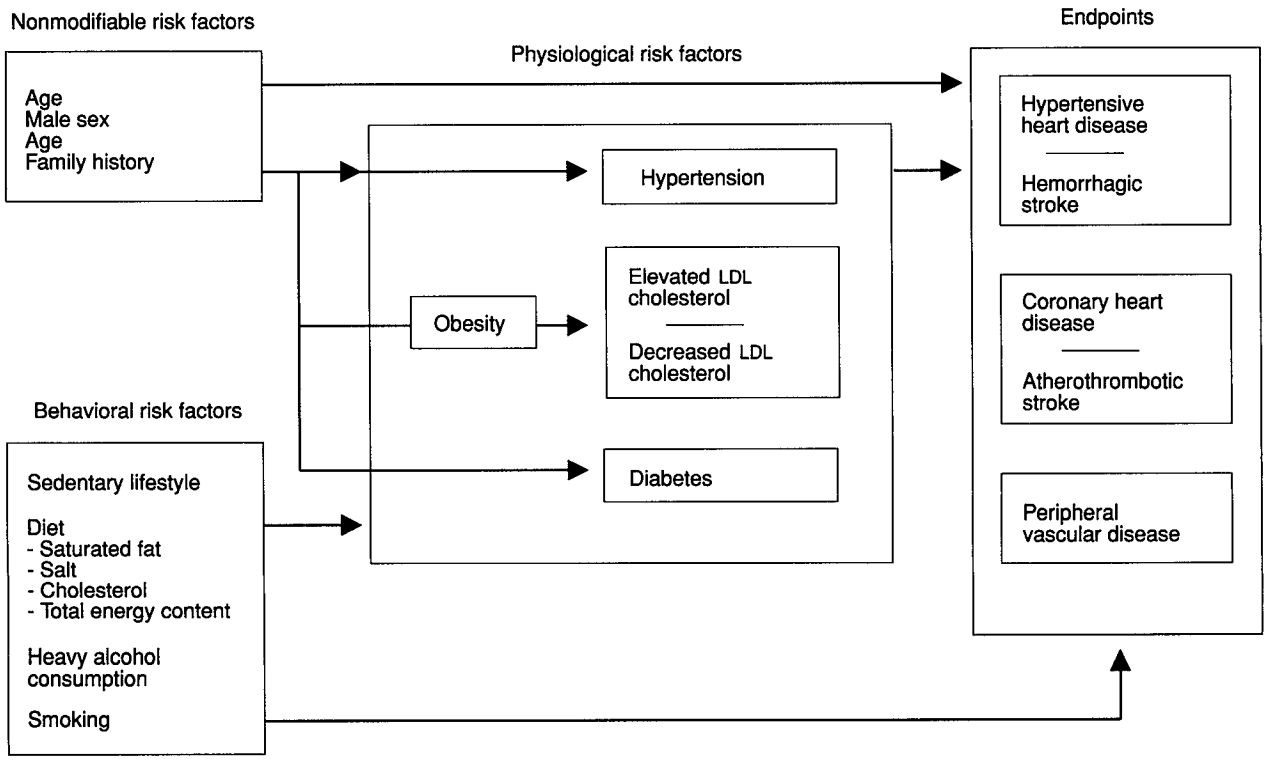
Coronary heart disease mortality rates increased in North America and Western Europe until the late 1960s and early 1970s, since which time they declined—a trend continuing today. The data are much different for Eastern Europe, where cardiovascular disease rates have increased steadily without evidence of stabilization or decline (Feinleib 1984; Thom and others 1985; Uemura and Pisa, 1988; Thom 1989; see table 23-3).

Rates in the developing world are much less well documented. Urban China, for example, appears to be experiencing a similar rise in coronary heart disease (Wu and others 1984; Tao and others 1989). Other developing countries appear to have similar rises in coronary heart disease rates (the reasons are discussed later). A significant exception is the recently documented experience of the city of São Paulo, Brazil, which, during the period 1970–83, experienced a 28 percent decline in mortality from ischemic heart disease and a 16 percent decline in deaths from stroke for the age group forty through sixty-nine (de Lolio and others 1986). These reductions were from quite high initial levels, so the pattern is like that of many of the industrial market economies.

STROKE. Because the presentation of hemorrhagic and atherothrombotic stroke appears similar clinically and developing countries may not have the technology to estimate their occurrence separately, their importance will be discussed together. In the United States, approximately 70 percent of strokes are atherothrombotic, with an additional 12 percent hemorrhagic (Schoenberg 1979). An additional 10 percent are made up of subarachnoid hemorrhage and other stroke syndromes. In Asia, the occurrence of intracranial hemorrhage is higher, with 50 percent of strokes being atherothrombotic and 40 percent being hemorrhagic.

The type of stroke is an important distinction, in that the mortality and prognoses differ (Marquardsen 1986). No more

Figure 23-4. Relationships among Risk Factors for Cardiovascular Disease



Source: Authors' compilation.

than 30 percent of those who suffer atherothrombotic stroke will die in the following three weeks; the prognosis for those with hemorrhagic stroke is worse, with case-fatality rates of 60 to 85 percent. Overall, 20 to 30 percent of stroke victims suffer major disability; only 50 percent to 75 percent are able to walk unaided. Again, primary prevention appears to be the logical target for intervention.

HYPERTENSIVE HEART DISEASE. Estimates of the prevalence of hypertensive heart disease have been difficult because of the aggregation of hypertensive heart disease with coronary heart disease in the International Classification of Disease. Because congestive heart failure and sudden death can be due to a variety of causes, including coronary heart disease, estimates of this condition are imprecise. Yet, in some countries, especially those with low atherosclerotic prevalence (for example, China), this condition appears to be an important cause of morbidity and mortality (Nissinen and others 1988, Hutt and Burkitt 1986). Blacks residing either in Africa, North America, or Europe consistently appear to have earlier onset, higher levels, and more severe cardiac sequelae than do whites ("Hypertension in Blacks and Whites" 1980; Falase 1987). Blood pressure control appears to be the main thrust of primary prevention; growing evidence suggests potential for regression of left ventricular hypertrophy with control of blood pressure.

The Burden of Cardiovascular Disease

This section reviews the effects of increased incidences of cardiovascular disease on current mortality levels.

Current Levels of Mortality

In table 23-4 we show rough demographic estimates, globally and by region, of the burden of mortality, in 1985, due to vascular diseases. In the table in appendix 23A we provide more detailed information on sex differences. It is evident from table 23-4 that death rates, and even proportion of deaths, due to circulatory disease are already very high indeed in Africa and Latin America and quite significant in Asia. Although the demographic assessments in table 23-4 are strongly suggestive of current levels of the mortality burden from CVD in different regions of the world, it is essential to bear in mind the substantial uncertainty surrounding the numbers in that table. They rely, for most of the developing countries, not on good national cause-of-death data but, rather, on extrapolations to the developing countries today of the experience of other countries, mostly European, from a time when their mortality levels were lower. It is therefore useful to supplement those extrapolations with examples from developing countries for which data do exist, and in table 23-5 we summarize such data from a number of sources.

Table 23-3. Change in Death Rates from Coronary Heart Disease, Selected Countries, 1969–78 and 1979–85
(percent)

Country	Men		Women	
	1969–78	1979–85	1969–78	1979–85
Australia	–24	–25	–25	–26
Austria	4	–11[a]	–6	–14[a]
Belgium	–13	–16[b]	–24	–7[b]
Canada	–14	–24	–21	–22
Czechoslovakia	8	12	2	16
Denmark	14	–14	1	–16
England and Wales	5	–12	9	–6
Finland	–8	–16	–18	–23
France	4	–4	–21	–2
Former Fed. Rep. of Germany	3	–10	–3	1
Hungary	37	27	21	23
Ireland	12	–7[b]	–10	3[b]
Israel	–22	–20	–19	–28
Italy	13	–10[c]	–7	–11[c]
Japan	–22	–20	–37	–27
Netherlands	1	–3	–2	–9
New Zealand	–13	–20	–16	–21
Norway	–5	–16	–11	–6
Northern Ireland	18	–18	28	–16
Poland	77	21[a]	71	26[a]
Portugal	2[d]	–15[a]	–11[d]	–5[a]
Scotland	3	–14	2	–7
Spain	53	—	29	—
Sweden	19	–12	–12	–19
Switzerland	10	–13	–7	–17
United States	–25	–22	–24	–15
Yugoslavia	32	15[c]	11	–2[c]

— Not available.
Note: Death rates are for men and women aged 45–64.
a. 1980–86.
b. 1979–84.
c. 1979–83.
d. 1971–78.

Trends to 2015

It is likely that all the important cardiovascular diseases will increase sharply in their morbidity and mortality between now and the years 2000 and 2015. Assumed in these conclusions is the control of major childhood and infectious diseases, with concomitant increase in population, life expectancy, and standard of living. The epidemiologic transition from infections to degenerative diseases as the main causes of death may be divided into at least four stages (table 23-6). A progressive change in risk factors and concurrent change in cardiovascular diseases is suggested by international comparisons of risk-factor prevalence and cardiovascular mortality in industrial countries (see table 23-3 and Knuiman and others 1980; Masironi and Rothwell 1988; Nissinen and others 1988; Uemura and Pisa 1988; WHO MONICA Project 1988). It is predicted that coronary disease, stroke, or hypertensive heart disease will be the leading cause of death for many developing countries by the year 2000. This will very likely be true even where age-specific death rates from CVD are declining, as they already are in parts of the developing world (for example, São Paulo [see de Lolio and others 1986]); where age-specific rates are rising—as they are for ischemic heart disease in Mexico (Lozano-Ascencio and others 1990)—the increasing prominence of CVD will be more pronounced. This will be particularly true of the managerial and professional classes in those countries. The trend toward the increasing importance of these diseases is dramatically illustrated in table 23-7.

EFFECT OF INCREASE IN LIFE EXPECTANCY. The crude incidence and prevalence of cardiovascular diseases must increase as life expectancy increases. This so-called "epidemiologic conversion" predicts such a rise in chronic disease rates as a function of life expectancy (Dodu 1988). Because coronary disease occurs even in people in their forties, it could represent significant burdens from those who are younger.

Another effect of increased age will be an increased prevalence of risk factors which may require control. Hypertension and elevated cholesterol are both examples of risk factors that become increasingly prevalent as age increases in most industrial countries, although these age-related increases may not be inevitable.

EFFECT OF INCREASE IN STANDARD OF LIVING. An increased affluence of population, if it were to occur, would have several possible effects on cardiovascular disease rates. First, an improved diet may also increase saturated fat, dietary cholesterol,

Table 23-4. Estimated Mortality from Circulatory System Diseases, by Region, 1985

Region	Deaths (thousands)	Total deaths (percent)	Age-standardized death rate (per 100,000 population)[a]		
			Total	Ischemic disease	Cerebrovascular disease
Industrial market economies	3,355	46	235	99	59
Industrial nonmarket economies	2,220	47	357	164	106
Latin America and the Caribbean	691	22	222	69	57
Sub-Saharan Africa	756	10	273	85	74
Middle East and North Africa	602	14	250	82	68
Asia	3,841	17	195	46	91
Total	11,466	23	243	84	81

Note: Constructed from the figures used by Bulatao and Stephens in tables 3 and 4 for "ischemic heart disease," "cerebrovascular disease," and "other cardiovascular." The total deaths in this table refer to the sum of these three categories, not to Bulatao and Stephens' "circulatory" category.
a. Rates are standardized using the 1985 world age structure.
Source: Bulatao and Stephens 1990.

Table 23–5. Age-Standardized Mortality from Vascular Diseases in Men in Selected Industrial and Developing Countries

Country	Annual mortality rate (per 100,000 population): Ischemic heart disease	Cerebrovascular disease	Ratio of ischemic heart disease to stroke
Industrial			
Canada	276	61	4.5:1
Japan	53	122	0.43:1
Portugal	108	240	0.45:1
United States	274	59	4.6:1
Former U.S.S.R.	486	245	2.0:1
Developing			
Brazil (São Paulo)[a]	310	198	1.6:1
China (Beijing)[b]	124	—	1:5[c]
China (Guangzhou)[b]	42	—	1:5[c]
Mauritius	123	94	1.3:1
Costa Rica	65	26	2.5:1
Cuba	168	65	2.6:1

— Not available.
a. Age group forty through sixty-nine.
b. Age group thirty-five through seventy-four.
c. For China as a whole.
Source: WHO 1988b, 1989; Tao and others 1989; de Lolio and others 1986.

calories, sodium, and alcohol, leading to increases in blood cholesterol, body weight, and blood pressure. For example, increases over time in dietary cholesterol, dietary fat, meat consumption, and cigarettes smoked per adult all correlated with increases in coronary heart disease in industrial countries (Byington and others 1979; Blackburn 1989; Epstein 1989). Sodium consumption correlates significantly with blood pressure levels in a recent study of fifty-two centers worldwide (Intersalt Cooperative Research Group 1988). Second, increased use of transportation and increased mechanization of industry may increase the prevalence of sedentary lifestyles. Third, increased affluence may increase cigarette consumption; indeed, in the companion piece on cancer in this collection (chapter 21), Barnum and Greenberg report enormously high income elasticities of consumption of tobacco products, particularly among the countries with the lowest incomes. Another, but favorable, effect of increased standard of living may be the improved cold storage of food, which has been suggested as the cause for the decline in strokes since 1900. The reduced requirement for smoked and salted foods may reduce the sodium content, resulting in reduced hypertension.

An increase in medical care services may also provide opportunity for reduction in cardiovascular disease rates. The disbursement of funds for preventive as opposed to acute care services, however, may determine the extent to which morbidity and mortality are reduced.

The Economic Burden of Cardiovascular Disease

Analyses of the economic burden of disease in developing countries are currently unavailable. It may, however, be suggestive to summarize findings on the burden of circulatory system disease in the United States based on one recent analysis (Rice, Hodgson, and Kopstein 1985). The authors of this analysis found that the direct cost of illness (that is, the cost of providing care) was $211 billion in 1980; given a gross national product (GNP) of approximately $2.6 trillion, this amounted to 8.1 percent of GNP. Of direct costs, about 15.4 percent were for circulatory diseases, so the cost of caring for these diseases was about 1.25 percent of GNP. The indirect costs of all disease (productivity loss due to morbidity and premature mortality) were slightly more, about 9.4 percent of GNP; for circulatory disease, the indirect costs were about 2 percent of GNP. Two points are notable: first, at a cost of more than 3 percent of GNP, circulatory disease imposes an enormous economic burden. Second, because deaths due to circulatory system disease were about 47 percent of total deaths, and its cost was less than 20 percent of the total costs of illness, the burden of circulatory illness is relatively much less measured in economic terms than mortality ones.

Analyses of this sort are sensitive to alternative assumptions and methodologies, and transfer of results from the U.S. situ-

Table 23-6. Circulatory System Disease at Phases of the Epidemiologic Transition

Phase of epidemiologic transition	Deaths from circulatory disease (percent)	Circulatory problems	Risk factors
Age of pestilence and famine	5–10	Rheumatic heart disease; infectious and deficiency-induced cardiomyopathies	Uncontrolled infection; deficiency conditions
Age of receding pandemics	10–35	As above, plus hypertensive heart disease and hemorrhagic stroke	High-salt diet leading to hypertension; increased smoking
Age of degenerative and man-made diseases	35–55	All forms of stroke; ischemic heart disease	Atherosclerosis from fatty diets; sedentary lifestyle; smoking
Age of delayed degenerative diseases	Probably under 50	Stroke and ischemic heart disease[a]	Education and behavioral changes leading to lower levels of risk factors

Note: Omran 1971 introduced the concept of epidemiologic transition with discussion of phases 1, 2, and 3. Olshansky and Ault 1986 added the concept of a fourth phase.
a. At older ages. Represents a smaller proportion of deaths.
Source: Omran 1971; Olshansky and Ault 1986.

Table 23-7. Ratio of Deaths from Circulatory System Diseases to Deaths from Infectious and Parasitic Diseases, by Region and Year

Region	*1970*	*1985*	*2000*	*2015*
Industrial market countries	5.63	6.64	9.61	11.88
Industrial nonmarket countries	2.44	4.72	5.24	4.41
Latin America and the Caribbean	0.68	1.09	2.46	4.74
Asia	0.42	0.60	1.55	2.75
Middle East and North Africa	0.37	0.41	0.81	1.26
Sub-Saharan Africa	0.23	0.27	0.38	0.54
Total	0.69	0.89	1.62	2.39

Source: Bulatao and Stephens 1990.

ation can, at best, be suggestive. That said, until country-specific analyses from developing countries are available, these estimates do probably serve as a reasonable first approximation of the cost of CVD (in percentage of GNP) for middle-income developing countries.

Strategies for Preventing Cardiovascular Disease

The preventive strategies, along with their cost in manpower, technology, and drugs, are listed for coronary heart disease, stroke, and hypertension in table 23-8. The preventive strategies are divided into public health (community-based) and high-risk (clinic-based) strategies. Several conclusions can be reached. First, several of the public health interventions are effective, including smoking cessation. The recent reviews by Warner (1989, 1990a) and the Surgeon General ("Reducing the Health Consequences of Smoking" 1989) of antismoking campaign effectiveness in the United States are encouraging in this regard. The Surgeon General's report, for example, summarizes evidence on the potent effect of taxes on tobacco products, particularly in the young and particularly with respect to initiation of use. The estimated price elasticity of demand is a substantial –0.42 for adults and a dramatic –1.2 for twelve- to seventeen-year-olds. In what is perhaps the first study of the price (actually, tax level) elasticity of tobacco consumption from a developing country, Chapman and Richardson (1990) found stronger elasticities in Papua New Guinea than in the United States. Efforts to promote low-fat diets and active lifestyles are also probably effective. Second, the public health interventions are often not costly. Much of the cost for community-based cardiovascular interventions may constitute the use of manpower, depending on the nature of the intervention. Many developing countries have a relative abundance of workers, including those with some training, which can be applied to these tasks. The technology and drug requirements for these strategies are low. Third, the ability to shift the risk of an entire population is calculated to have more promise in the prevention of the majority of deaths than does the treatment of high-risk individuals (Kottke and others 1985; Fries, Green, and Levine 1989; Gunning-Schepers and others 1989), although arguments to the contrary have been presented (Oliver 1984; Lewis and others 1986; McCormick and Skrabanek 1988). The current policy of the World Health Organization, which is to emphasize primordial prevention in developing countries, is predicated on a broad consensus among experts that a community-based strategy is feasible (WHO 1982). Finally, all the community-based strategies might be carried out in clinical settings, so that the community-based and clinic-based strategies are overlapping, rather than exclusive.

The high-risk, or clinic-based, strategy does include several effective interventions, however. Lipid-lowering drugs, for coronary disease and peripheral vascular disease, and antihypertensive drugs, for stroke, hypertension, and coronary disease, are clearly effective (MacMahon and others 1990). With the exception of antihypertensive therapies, it has been difficult to attribute recent declines in coronary disease in industrial countries to the medical management of risk factors (Pearson 1989). These strategies will often require large numbers of well-trained workers, however, as well as technology in the form of laboratories to monitor effects and side effects of therapy (for example, lipid laboratories to monitor serum potassium levels). Drugs can also be relatively expensive, although there are a number of important antiplatelet, antidysrhythmic, and antihypertensive drugs (for example, verapamil, propranolol, and hydrochlorothiazide) available through the World Health Organization/United Nations Children's Fund (WHO/UNICEF) Essential Drugs program at costs of under $5 per patient per year (UNICEF 1989). It should be emphasized, however, that a wide range of costs exists for drugs, from inexpensive lipid-lowering (for example, nicotinic acid) and antihypertensive agents (for example, reserpine) to expensive drugs (HMG-CO-A [3-hydroxy-3 methylglutaryl coenzyme A] reductase inhibitors, angiotensin converting enzyme inhibitors). Aspirin, which is extremely inexpensive and widely available, plays a potentially central role through its antiplatelet effects. Antiplatelet drugs may be effective in the primary prevention of coronary disease but not stroke (Hennekens and others 1989).

It should be pointed out that the relationship between the population-based and high-risk strategies remains to be assessed; nonetheless, the European Atherosclerotic Society (1987) has noted that it seems highly probable that the two strategies would be mutually supportive. Along these lines, Rothenberg, Ford, and Vartiainen (1990) have undertaken a multirisk-factor modeling exercise that suggests that overall preventive strategy may well focus on high-risk groups for some risk factors and whole populations (probably age targeted) for others, depending on specific characteristics of available interventions.

It is not likely that new technologies available for public health interventions will become available. Knowledge regarding the beneficial effects of lipid-lowering diets, exercise,

Table 23-8. Efficacy and Cost of Preventive Strategies for Major Cardiovascular Diseases

Preventive strategy	Effectiveness		Costs		
	Compliance	Clinical efficacy	Manpower	Technology	Drugs
Coronary heart disease					
Community-based					
Smoking cessation	+	++++	+/–	0	0
Low-salt diet	+	?	+/–	0	0
Modified fat diet	+	+++	+/–	0	0
Exercise	+	+++	+/–	0	0
Diabetic diet	+	—	+/–	0	0
Obesity control	–	?	+/–	0	0
Clinic-based					
Antihypertensive drugs	+	++	++	+	++
Lipid-lowering drugs	+/–	++++	++	++	++
Diabetic drugs	+	—	++++	++	++++
Antiplatelet drugs	++	++	+	+	+
Stroke					
Community-based					
Smoking cessation	+	+++	+/–	0	0
Low-salt diet	+	+	+/–	0	0
Obesity control	–	+	+/–	0	0
Clinic-based					
Antihypertensive drugs	+	++++	++	+	++
Antiplatelet drugs	++	++++	+	+	+
Hypertension					
Community-based					
Low-salt diet	+	+	+/–	0	0
Exercise	++	++	+	0	0
Obesity control	–	+++	+/–	0	0
Alcohol restriction	?	+	0	0	0
Clinic-based					
Antihypertensive drugs	+/++	++++	++	+	++

Key: ++++ Highly favorable.
+++ Moderately favorable.
++ Favorable.
+ Minimal.
+/– Variable.
– Poor.
— Not effective.
0 Not required.
? Unknown.

Source: Authors' compilation.

and sodium restriction, however, should continue to increase. For example, results are now being published from the study undertaken by the Intersalt Cooperative Research Group (1988) in thirty-two countries, including twelve developing countries, of the prevalence of hypertension and its association with sodium, potassium, and alcohol intake. Community intervention strategies that will probably be generalizable to developing countries are now being implemented in the United States and Europe (Blackburn 1983).

A number of changes will likely occur with physician-based preventive strategies (Pearson 1989). New antihypertensive drugs with better treatment schedules and fewer side effects are constantly being developed. It is hoped that inexpensive, low side-effect, and once-a-day dosing drugs will become available. New techniques for detection of high blood cholesterol are being implemented but are probably too costly for most developing countries at present prices (Weinstein and Stason 1985). Diabetic drugs, including new insulin delivery systems, are being evaluated for efficacy. Again, these are high-technology instruments, usually with high unit costs.

The Gap between Good Practice and Actual Practice

Many, or perhaps most, countries, industrial or developing, have not enacted national policies intended to prevent the use of tobacco products. Further, few countries encourage low-fat, low-cholesterol, low-salt diets; indeed, few countries have a national nutrition policy of any kind. Exercise and fitness are variably encouraged in schools and work sites. Thus, a number of public health or regulatory policies need to be implemented.

Physicians in industrial countries remain oriented toward acute care, rather than preventive care. Many health messages are therefore not delivered at the time of the acute care visit (for example, an antismoking message). Thus, risk factors in the high-risk patient are often not detected or treated.

In judging the potential for improving practice, assessments of the cost-effectiveness of alternative strategies for prevention provide potentially useful guides. Weinstein and Stason (1985) provide a valuable introduction to the relevant literature that was available at the time of their writing; that literature is limited, unfortunately, to studies from high-income countries. Further, we have been unable to find any studies assessing community-based interventions; the closest was a study of screening of hypertensives followed by their treatment in North Karelia, Finland. The authors of the North Karelia assessment estimated the cost per (disability-adjusted) year of life gained to be about $3,600 (Nissinen and others 1986). Weinstein and Stason reported that in earlier studies on hypertension control rather more costly, although not markedly higher, results had been found. Naturally, the cost per year of life gained falls as the cutoff level for treatment of blood pressure rises—but with concomitant loss of some lives that would have been saved were the cutoff level lower. In a recent study, Hatziandreu and others (1988) assessed the cost-effectiveness of exercise as a preventive measure for ischemic heart disease, finding costs of about $11,000 per disability-adjusted year of life saved. The main cost is that of the time taken for exercise and that "cost" is itself highly dependent on whether exercise is a pleasure; the authors assumed that, on average, it was not.

Much of the work on the cost-effectiveness of prevention has addressed the attractiveness of efforts to reduce serum cholesterol. Taylor and others (1987) put forward an often-refuted model linking changes in cholesterol levels to changes in life expectancies for varying initial ages and cholesterol levels; the results provide the effectiveness measures that can be used in cost-effectiveness analyses and suggest very little benefit (several months' gain in life expectancy) for lifelong programs to lower cholesterol by typical dietary means. More substantial gains result from the potent effect of cholesterol-lowering drugs, but an early analysis of the cost per year of life gained from the use of cholestyramine resulted in high estimates, in the region of $125,000 (Weinstein and Stason 1985). In a still earlier assessment of a pediatric screening program followed by dietary management, Berwick, Cretin, and Keeler (1980) found much more modest costs—in the region of $10,000. Kinosian and Eisenberg (1988) assessed several agents in their investigation into the medical management of cholesterol. Their findings on cholestryamine were similar to those of Weinstein and Stason, but they found that the use of oat bran resulted in much lower costs—about $18,000 per year of life saved, which is still expensive in relation to the hypertension control efforts assessed.

The purpose of these assessments is to help guide resources toward uses that buy the greatest possible gain in disability-adjusted life-years for the money available. They do not, in this case, point more sharply in one direction than another; rather, they suggest adjustments of treatment cutoff points (hypertension cutoffs down, cholesterol cutoffs up) to maximize health gains. Further, for developing countries, these costs are high; later we suggest that care taken in implementation could lower costs in developing countries.

Suggested Intervention in a Standardized Population

A concerted effort through public education, including that in the schools, work sites, and media, should be carried out to reduce the prevalence of smoking. Regulations to restrict smoking from work sites, public places, and the like might be enacted. The sale of cigarettes might be heavily taxed. Nutritional programs to provide low-fat, low-cholesterol sources of protein should be enacted. The use of nonsaturated fat in cooking oils should be encouraged. Facilities and encouragement for exercise should be made policy at schools, work sites, and public places. The use of personal transportation might emphasize expenditure of calories for the nonpoor population subgroups.

As health care strategies, all adults might have their blood pressure taken, and those in whom it is found to be elevated might begin a weight loss, salt-restricted diet with appropriate physician follow-up, including the use of inexpensive antihypertensive agents. Cholesterol screening might be restricted to persons with relatives who have developed cardiovascular disease at age fifty years or less. Follow-up and treatment would require dietary restrictions of fats and cholesterol, and possibly low-cost medicines to lower cholesterol.

We have made several tentative calculations to estimate probable cost and effect, in the hypothetical population of 1 million, of several preventive interventions—a general public preventive package (education, screening, counseling, referral), a program to control hypertension, a program to control hyperlipidemia, and a 20 percent tax on tobacco products. Our preliminary estimates, which assume low-cost medications (such as propranolol purchased at prices on the *Essential Drug List* [UNICEF 1989]), are as follows:

- For hypertension control, perhaps 90 deaths per year could be averted at a cost of about $2,000 per year of life gained
- For hypercholesterolemia control, somewhat fewer deaths could be averted at a cost of about $4,000 per year of life gained
- Assuming that a public preventive package could be implemented for about half the cost as in the United States (that is, for about $0.75 per capita per year) perhaps 250 lives per year could be saved at a cost of about $150 per year of life gained
- A 20 percent tobacco tax would reduce consumption by about 20 percent and free resources for other uses. Assuming that there were 200,000 smokers in the population of 1 million and that the health effect was as though 40,000 people stopped smoking and others did not change behav-

ior, perhaps 40 deaths per year from coronary artery disease would be averted.

Calculations of this sort will, obviously, give quite different results in different epidemiological and health service environments; and even these estimates for a hypothetical population should be viewed as tentative. Nonetheless, these estimates do give a rough sense of the cost-effectiveness that might be expected for several key interventions.

Case Management of Cardiovascular Conditions

The potential elements of case management strategies are listed in table 23-9 and are separated into acute and chronic interventions. Several conclusions can be drawn. First, the acute interventions are often not extremely effective when tested in clinical trials (for example, antiarrhythmic drugs such as lidocaine, coronary care units, cardiopulmonary resuscitation, calcium channel blockers; see MacMahon and others 1988; Yusuf, Wittes, and Friedman 1988a; Held, Yusuf, and Finberg 1989). Second, these acute interventions are costly with regard to manpower, technology, and drugs. Third, the effectiveness of some chronic interventions is perhaps better, with more widespread application feasible. Again, several interventions such as angioplasty and bypass surgery are costly; even so, targeted interventions (for example, coronary artery bypass surgery [CABS] for left main coronary artery disease only) can be cost-effective, at least in industrial countries (Williams 1985). Certain interventions, such as smoking cessation, lowering of serum cholesterol, and exercise in cardiac rehabilitation, show promise of being effective at low cost (Oldridge and others 1988; Yusuf, Wittes, and Friedman 1988b; "The Surgeon General's 1990 Report on the Health Benefits of Smoking Cessation" 1990). It is further logical that chronic risk factor intervention may be more effective in populations also in community-based programs.

It is further predicted that the classes with greater education and income may demand this high-technology care, obtained in their home countries or by traveling to an industrial country. Because it is these classes that will develop cardiovascular disease first in a country, extreme pressures will likely be exerted to develop high-technology health care. It is probable that for this reason a small amount of this high technology will be needed in all countries. Nonetheless, a key element of overall strategy will be to make low-cost but effective alternative interventions regularly available. In many cases, these options do exist.

The field of interventional cardiology is rapidly changing, with the advent of new therapies for the patient with angina pectoris, myocardial infarction, stroke, or peripheral vascular disease. Most invasive strategies (for example, laser angioplasty) and those involving new drugs (new thrombolytic agents, free radical scavengers, and so on) are likely to be costly in manpower, technology, and drugs. A full description of potential advances is beyond the scope of this review.

Gaps between Good Practice and Actual Practice

It appears likely that some of the new technology will improve case-fatality rates. Many institutions, however, even in the industrial countries, cannot afford its implementation. There also appears to be a lack of attention to some of the rather simple chronic interventions (smoking cessation, cardiac rehabilitation, beta-blocker therapy) which have been shown to be related to improved chance of survival in patients with CHD. Thus, an improved use of these interventions may increase survival rates. Cost-effectiveness studies for several of these strategies have been attempted, including bypass surgery, use of beta blockers after myocardial infarction (MI), coronary care units, and cardiopulmonary resuscitation programs (Weinstein and Stason 1985). More recently, Steinberg and others (1988) examined the use of thrombolytic therapy in treating acute MI. Most of these strategies are expensive (upward of $30,000 per year of life saved), although CABS for left main coronary artery disease and three-vessel coronary artery disease is a relatively cost-effective treatment in high-income countries, at costs well under $10,000. Risk stratification appears able to identify patients who have especially attractive cost-benefit ratios; Goldman and others (1988) estimate beta-blocker therapy to cost from $23,400 per year of life saved in low-risk patients to $3,600 per year of life saved in high-risk patients.

Suggested Intervention in a Standardized Population

Four interventions appear worthy of serious consideration—risk reduction in post-MI patients, risk management in poststroke patients, angina control, and low-cost management of acute MI. These are discussed below.

For both the post-MI and poststroke patients, emphasis on the modification of risk factors should be made, including the control of hypertension in the stroke victim; the cessation of smoking in the coronary, cerebrovascular, and peripheral vascular patient; and the lowering of blood cholesterol by diet or inexpensive drugs. For the patient with chronic cardiovascular disease, rather inexpensive drugs might be used for the treatment of angina or following myocardial infarction (for example, beta blockers; see Julian 1989). Antiplatelet agents, particularly aspirin, may be helpful in patients with coronary artery disease, and atherothrombotic but not hemorrhagic stroke. These low-cost secondary preventive measures for this high-risk group might cost $3 per patient per year, if carefully implemented. They might be expected to reduce the annual probability of death by 0.01 or 0.02 for an age group in which a death would result in loss of, perhaps, fifteen discounted (at 3 percent) life-years for the post-MI patient and ten years for the poststroke patient. This would result in a cost per disability-adjusted life-year gained of $155 for intervention in the post-MI group and $230 in the poststroke group.

Of particular importance in case management is the cost-effectiveness of angina control medication, which is inexpensively available from the WHO/UNICEF Essential Drugs program. It is estimated that the standard population would have about

Table 23-9. Effectiveness and Cost of Case Management Strategies for Cardiovascular Disease

Case management strategy	Efficacy	Costs		
		Manpower	Technology	Drugs
Coronary heart disease				
Acute MI/unstable angina				
Cardiopulmonary resuscitation	+/–	+++	+++	+++
Coronary care units	+	++++	++++	+++
Antiarrhythmic drugs	–	+ +	+ +	+++
Thrombolysis	+ +	++++	++++	++++
Nitrates	+ +	+/+++	+	+/+++
Antiplatelet/anticoagulant drugs	+ +	+	+	+
Chronic angina/stable post-MI				
Beta-blocking agents	+++	+++	+	++++
Calcium channel blockers	0	+++	+	++++
Angioplasty	?	++++	++++	+ +
Coronary artery bypass surgery	+	++++	++++	+ +
Antiarrhythmic drugs	–	+++	+ +	++++
Cardiac rehabilitation (including smoking cessation)	+++	+++	+	0
Antiplatelet agents	+ +	+	0	+
Cholesterol-lowering drugs	+ +	+ +	+++	++++
Congestive heart failure				
Drug therapy	+	++++	+++	++++
Heart transplantation	+ +	++++	++++	++++
Stroke				
Acute stroke				
General support	?	+++	+ +	0
Stable poststroke/transient ischemic attack				
Antiplatelet agents	+ +	+	0	+
Antihypertensive drugs	+++	+ +	+	+++
Carotid surgery	?	+++	++++	+
Peripheral vascular disease				
Acute				
Surgery	+ +	+++	++++	+ +
Chronic				
Surgery/angioplasty	+ +	++++	++++	+ +
Smoking cessation	+++	+	0	0
Hypertensive disease				
Congestive heart failure				
Drug therapy	+/–	++++	+++	++++
Hypertensive renal disease				
Dialysis	+ +	++++	++++	+ +

Key: ++++ Very high.
+++ High.
++ Moderate.
+ Minimal.
– Not effective.
+/– Variable.
0 Not required.
? Unknown.

Source: Authors' compilation.

6,000 cases of moderate to severe angina at any given time, which could be medically controlled for perhaps $150,000 to $200,000 per year. If, consistent with Weinstein and Stason, we use a Q factor of 0.7 to 0.9 for angina (that is, between 0.1 and 0.3 years of healthy life are assumed to be lost per angina-affected person per year), the cost per disability-adjusted year of life gained from angina control would be only $100 to $200.

Table 23-9 contains a range of options for management of acute MI and unstable angina. Many of these are highly costly, and some are of limited or unproven effectiveness. One strategy of medical intervention, however, would be relatively

easily managed and involve only very low cost drugs—nitroglycerin and aspirin (as an antiplatelet agent). Pitt (1989) suggested that at least some of the reduced case-fatality rates for MI observed in industrial countries during the past two decades may be attributed to these agents. Patients presenting with acute MI would be provided these medications (and supportive care) on an inpatient basis for several days. The drug cost would be close to negligible; depending on local circumstances, the cost of hospital stay and physician time might be in the range of $100 to $250. Intervention of this sort might reduce the short-term mortality risk from 20 to 15 percent, resulting in a gain of 0.75 disability-adjusted life-years (again assuming that a death averted at about this age will result in a gain of fifteen disability-adjusted life-years). The resulting cost-effectiveness would, then, be in the range from $135 to $335 per disability-adjusted life-year gained.

The above cost-effectiveness estimates can be considered only approximate; much more careful analyses could (and should) be done in country-specific circumstances. The estimates of cost and effectiveness are, nonetheless, within reasonable ranges; the resulting cost-effectiveness estimates serve to give a realistic (if approximate) sense of what is possible.

In table 23-10 we summarize the range of case management options for vascular disease with regard to their objectives (secondary prevention or rehabilitation) and the sophistication of the probable venue for the intervention. Priority interventions tend to be those that can be delivered in less sophisticated environments, such as those described in more detail in the preceding paragraphs.

Conclusions and Priorities

We have attempted to summarize available data and analyses concerning the epidemiology of cardiovascular diseases in developing countries, strategies of prevention, and methods of case management. Imbalances in the available literature are striking: there is a vast medical and epidemiological literature on cardiovascular disease, but almost none of it deals with problems of developing countries, where well over half of cardiovascular mortality occurs. Likewise, although cardiovascular disease already accounts for 10 to 35 percent of all deaths in developing countries (and, soon, will account for a much higher percentage), the substantial literature on epidemiology and health planning for developing countries concentrates almost exclusively on communicable diseases, particularly the communicable diseases of childhood. Nonetheless, for a few developing countries, and in a preliminary way, explicit consideration has begun of the implications for health policy of the increasing prominence of chronic diseases; for example, for China (Jamison and others 1984), for Malaysia (Harlan and others 1984), for Mexico (chapter 3, this collection), and for Brazil (de Lolio and others 1986, and ongoing World Bank work). Our purpose in this chapter has been to take stock of what literature does exist concerning cardiovascular diseases in developing countries as a starting point for further work.

The appropriate range of policy instruments to consider, as well as research priorities, will vary, of course, depending on the epidemiological and economic conditions in a particular country. Although many of those conditions are quite country specific, we have nonetheless found it useful to characterize the evolving nature of circulatory problems in a way that parallels the epidemiological transition; in table 23-6 we summarized this characterization. During the pretransition phase of high mortality, circulatory problems are of modest relative importance (although, perhaps, of substantial absolute importance); they are, in this phase, dominantly conditions of infectious origin, which we have not discussed in this chapter. As mortality declines, there appear to be, first, rising problems associated with the hypertension-related circulatory diseases; this stage is followed, perhaps substantially later, by diseases that are principally atherosclerotic in origin. (Indeed, the low levels of atherosclerotically related diseases in Japan today suggests the general possibility that a major epidemic of these diseases could be avoided in other parts of the world.) This phasing has important implications for the timing of the introduction of both preventive and case management interventions.

Table 23-10. Objectives and Venue for Case Management of Cardiovascular Disease

	Venue			
Objective	*Household*	*Primary facility*	*Secondary facility*	*Tertiary facility*
Secondary prevention				
Angina pectoris Myocardial infarction Stroke	Behavioral change: risk factor management; drug compliance	Simple diagnosis: prescription of first-line drugs[a]	Complex diagnosis;[b] second-line drugs[c]	Invasive diagnosis; surgical therapy; complex drugs and technologies
Rehabilitation				
Myocardial infarction Stroke	Habits of daily living; long-term, unsupervised exercise program	Monitored outpatient program	Supervised inpatient program; physical and occupational therapy	Specialized rehabilitative occupational therapy; prostheses, patient-assist devices

a. Propranolol, verapamil, aspirin.
b. Established through exercise electrocardiogram, echo-doppler examination, and similar technologies.
c. For example, long-acting nitrates, anti-arrhythmic drugs.
Source: Authors' compilation.

Operational Priorities for Developing Countries

The following steps might be appropriately emphasized as ones that developing countries might take to forestall (primordial prevention) or reduce the forthcoming epidemic of cardiovascular disease and to deal with its consequences. These interventions tend also to be appropriate for other chronic diseases, and the suggestions here are generally consistent with those of WHO's "Interhealth" program (Integrated Programme for Noncommunicable Disease Prevention and Control, Shigan 1988). The interventions are listed in order of priority for implementation.

PREVENTION. The range of appropriate preventive interventions in developing countries is similar to that for industrial ones and includes the following:

- Regulation, taxation, and education to reduce the production and use of tobacco products. These form perhaps the single most important cluster of preventive interventions. The potential benefits of this strategy are reviewed in more detail in appendix A of this collection, and Warner (1990b) emphasizes the particularly important role that taxation policy can play in limiting tobacco use in developing countries.
- National nutrition policies, including substantial use of taxes, to improve nutrition without the use of excess saturated fat, dietary cholesterol, salt, calories, and alcohol. These policies should be targeted at those segments of a society in whom malnutrition (that is, undernutrition) is not a problem. The prevention of obesity should be a major target of these programs.
- Screening for (probably in the context of other screening) and nonpharmacologic treatment of hypertension. Use of even relatively inexpensive antihypertensive drugs in those high-risk patients not responding to nonpharmacologic therapy is probably not cost-effective, except for individuals at very high risk. The drugs themselves are now quite inexpensive (UNICEF 1989); the cost issue is that of monitoring of response, side effects, and the compliance of patients with their treatment regimens. The large number of compliant individuals required per death averted is the limiting factor on cost-effectiveness.
- National fitness programs. Such programs should be emphasized for those segments of the population that have occupations or lifestyles which reduce their levels of physical activity, or those subgroups prone to obesity.
- Toward later stages of the epidemiologic transition, limited introduction of inexpensive antihyperlipidemics. These might be considered for individuals with very adverse lipid profiles; the WHO/UNICEF *Essential Drug List* should, therefore, be expanded to include an effective, inexpensive lipid-lowering agent (such as nicotinic acid). As with control of hypertension, however, but even more so, the large number of compliant individuals required to avert a death sharply constrains cost-effectiveness.

CASE MANAGEMENT. The range of cost-effective case management interventions is much narrower in developing countries than in industrial ones. They include the following:

- Post-MI and poststroke care. Improvement is needed in such care, with emphasis on modification of risk factors (for example, smoking) and inexpensive drug treatment (for example, beta blockers, aspirin).
- Low-cost drugs (propranolol, aspirin) and modification of risk factors for treatment of angina. Risk factor modification should include lipid-lowering diet or drugs, smoking cessation, and the like. Treatment of angina appears particularly cost-effective.
- An inexpensive (and cost-effective) protocol to treat acute MI and unstable angina. Such a protocol should emphasize the use of aspirin and nitroglycerin.
- Strict limitations on provision for (locally or abroad) invasive diagnostic (coronary arteriography) and treatment (coronary care units, coronary bypass surgery) facilities, with their use limited to the young, highest-risk subgroups of patients, and then only after the more cost-effective strategies just described have already been tried.

Operations Research in Developing Countries

The following are areas of priority for operations research, along the lines that Tanzania has initiated with the assistance of WHO (WHO 1986). Given the public health significance of cardiovascular disease in developing countries, and its rising absolute and relative importance, the current neglect of applied research is striking.

EPIDEMIOLOGY. Additional data on the distribution, causes, and national history of CVD is needed in the following areas:

- Better data must be sought on the incidence, prevalence, case-fatality rates, and prognosis of cardiovascular diseases to determine the circumstances under which development and increasing affluence result in increased age-specific cardiovascular disease rates.
- Better data must be sought on the prevalence of modifiable risk factors, especially in those countries with increasing cardiovascular disease rates.
- Better data must be sought on the relative risk and the attributable risk of risk factors in developing countries.
- Developing country participation must be greatly expanded in international programs of cardiovascular epidemiologic investigations and surveillance, such as MONICA, to provide standardized measurement techniques and numerous industrial countries for comparison.

RISK MODIFICATIONS. Little information is available on the effectiveness of interventions to lower the risk of CVD. Additional research is needed in the following areas:

- Research must be undertaken in community-specific and culture-specific strategies to use mass media, community

resources, and other modifiers of human behavior to alter the level of risk factors.

- The effectiveness of price and taxation policies in modifying the distribution of risk factors must be studied.
- Studies must be undertaken of the relative effectiveness and cost-effectiveness of both nonpharmacologic and drug interventions to reduce risk factors in individuals of that particular culture.

CASE MANAGEMENT. The management of established CVD also needs further investigation.

- Studies must be conducted of the relative effectiveness and cost-effectiveness of both nonpharmacologic and drug interventions to reduce case-fatality rates and to improve prognosis in patients with cardiovascular disease.
- Given that only very small numbers of expensive invasive procedures will be undertaken, research must be carried out concerning the economics of referral for these procedures and optimal location for them (including at centers abroad).

In this chapter we have assembled evidence that points to the large and growing significance of cardiovascular disease in developing countries; we have reviewed the range of available options for prevention and case management; and we have assessed the cost-effectiveness of a range of the most attractive intervention options. A number of broadly relevant interventions have been identified that, potentially, have cost-effectiveness measures from $150 to $350 per disability-adjusted life-year gained; although these figures are not the most attractive that Jamison (chapter 1 of this collection) has summarized for interventions addressing health problems of adults, they do fall at the low end of the range and should become integral to the range of services most countries provide. Interventions to reduce smoking are even more attractive, in part because they simultaneously reduce the risk of lung cancer and other conditions. Finally, it is worth stressing that many interventions of very low cost-effectiveness have also been identified; considerations of both efficiency and equity suggest that their use should be curtailed.

Appendix 23A. Cardiovascular Mortality Differentiated by Sex

MONICA data suggest a very strong effect for ischemic heart disease and a much weaker one for stroke among males.

Table 23A-1. Sex Differences in Age-Standardized Cardiovascular Mortality, Selected Populations, 1984

	Cerebrovascular disease				*Ischemic heart disease*			
Location	*Male mortality rate* (10^{-5})	*Female mortality rate* (10^{-5})	*Male/female ratio*	*Male/female ratio of proportional mortality*[a]	*Male mortality rate* (10^{-5})	*Female mortality rate* (10^{-5})	*Male/female ratio*	*Male/female ratio of proportional mortality*[a]
Perth, Australia	26	24	1.1	0.57	161	38	4.2	2.1
Bejing, China	98	82	1.2	0.96	40	28	1.4	1.3
Finland	60	42	1.4	0.46	374	57	6.6	2.1
Italy: Latina area	68	33	2.1	0.92	96	20	4.8	2.3
California	25	20	1.3	0.59	221	40	5.5	2.7

Note: Mortality rates are annual, for a population of 100,000 age thirty-five through sixty-four.
a. Obtained by dividing the percent of total mortality in males by the same percentage in females.
Source: MONICA Principal Investigators 1987.

Notes

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